

Update on the FSA's science activities on antimicrobial resistance including the report of the ACMSF task and finish group

Report by Steve Wearne

For more information, please contact Paul Cook
Email: paul.cook@food.gov.uk, Tel: 0207 276 8950

Summary

1. This paper provides an update on the FSA's science activities concerning antimicrobial resistance and the food chain since the Board paper in December 2017; it includes:
 - the report and recommendations of the ACMSF Task and Finish Group; and
 - the FSA's programme of research and surveillance in this area, which positions us well to respond to the Task and Finish Group's recommendations.
2. The Board is asked to:
 - **discuss** the report and key recommendations; and, in particular; and
 - **agree** that the report provides an evidence base to inform engagement with other partners including other research funders with whom we will need to work to deliver this agenda.

Introduction

3. Antimicrobial resistance (AMR) is a national strategic priority for government and the FSA is playing its part by continuing to fill the evidence gap on the role that food plays in AMR. Since the Board paper on AMR in December 2017, the FSA has been working with partners across government to help develop a refreshed AMR strategy with a "One Health" approach including a 20-year vision. Food safety will be a component of the new strategy and this will provide an opportunity to highlight the surveillance and research areas needed to improve the scientific evidence base concerning the role of food as a transmission pathway for AMR. The new strategy will also include the environment as a key component and we will need to consider areas where there is an interface with the food chain. Internationally the UK is contributing to the Codex Alimentarius Task Force on AMR which is revising the code of practice to help support everyone in the food chain to take actions to minimise and contain antimicrobial resistance. The Task Force is also developing guidelines on integrated monitoring and surveillance of foodborne AMR.

4. This paper presents an update on the Agency's science activities relating to AMR following the update provided to the Board in December 2017. This includes the report of the ACMSF Task and Finish Group on AMR (Annex 1) and a summary of the FSA's continuing programme of research and surveillance on AMR (Annex 2). The December 2017 paper followed the FSA Board's discussion on AMR in September 2016 where the Board position on AMR was set out, which is:
- to focus on improving the scientific evidence base relating to AMR in the food chain through supporting relevant research and by improving surveillance;
 - to encourage the adoption of clear transparent reporting standards that help consumers have access to and understand information about the responsible use of antibiotics in the food chain;
 - to ask the AMR subgroup of the ACMSF to advise us on responsible use of antibiotics in agriculture to support these two objectives; and
 - to play a leadership role in Codex in the area of AMR. We adopted these areas of focus as the most appropriate way to make our departmental contribution to the Government's strategy and action plan for tackling AMR.

Evidence and discussion

ACMSF fixed term Task and Finish Group report on AMR

Background

5. The Board agreed to the establishment of an ACMSF fixed term Task and Finish Group on AMR at its meeting in November 2016, with the aim of the group to produce an authoritative report.
6. The groups terms of reference were "To identify research questions and potential approaches which would (i) decrease uncertainty about any linkage between use of antimicrobials in food production, the incidence of antimicrobial resistance in pathogens and commensals in food production, and the growing AMR-related public health burden, and (ii) allow us to model the impacts of changes in use of antimicrobials in food production. Poultry, sheep, cattle and pigs will be covered in the scope."
7. The Task and Finish Group comprised of the existing ACMSF AMR subgroup, supplemented with additional AMR expertise to identify research questions and potential approaches for future research relating to antimicrobial resistance and the food chain. The group met five times during 2017 and the completed report was endorsed by the ACMSF in March 2018. The final report is at Annex 1.

Approach of the group

8. During a series of scoping discussions, the group worked closely with colleagues from FSA Microbiological Risk Assessment and Analytics, in reviewing the aspects of a cross governmental AMR systems map developed in 2014 that are relevant to the FSA, and in developing a detailed systems map focussing specifically on the food chain. This map guided the discussions and activities of the group, and identified eight main reservoirs with a potential AMR impact relevant to FSA, which were subsequently reviewed within the group's report. These are: Pasture & Crops; Amendments¹; Animal Feed; Food Producing Animals; Abattoir & Carcass Processing; Food Processing; and Human Food and Humans. As part of the review process, the group also received presentations on antimicrobial usage and AMR from a range of UK food animal production sectors (poultry, pigs, dairy and beef cattle, sheep).

Recommendations

9. The group made recommendations in the eight areas mentioned previously. Whilst the focus of the work included evidence gathering and recommendations related to the eight identified reservoirs, very early in their discussions, the group agreed that there is a significant and long-standing lack of antimicrobial and AMR data in relation to UK-produced, processed and/or imported food, both in absolute and comparative terms.
10. Recommendations considered as high priority for the FSA focused on priority areas of research and surveillance. Areas where information is already available and where the FSA's efforts could be re-directed were also flagged. The report also highlighted recommendations of lower priority for the FSA and where collaborative work is required with other government departments or organisations taking the lead.

High priority recommendations

11. Further research and surveillance is needed to continue quantifying the risk of transmission to humans of antimicrobial resistance genes, and particularly those encoding resistance to Critically Important Antimicrobials (CIAs), including plasmid-mediated colistin resistance in organisms from foods of both animal and non-animal origin, both UK-produced and imported. In this same area, the group recommended that regular targeted surveillance of specific food items for AMR is essential, including both foods of animal and non-animal origin, and both home-produced and imported foods.
12. Co-ordinated research is a high priority. The group suggested that FSA should continue to monitor the relative importance of AMR in food relative to other

¹ Amendments refer to waste-derived materials that are spread onto land for some benefit (usually agricultural). For example, materials containing nitrogen, potassium or other nutrients may enhance crop growth, but can also contain chemical or biological contaminants.

contributory factors. This stemmed from the observation that there appears to be a significant gap in the overall governance of research activity into antimicrobial resistance and food. At present, most research outputs appear to result from the intermittent availability of largely uncoordinated, opportunistic funding.

13. In the area of food processing, the group recommended that the FSA should commission as high priority, a research review on the impact of currently used sub-lethal food processing technologies in encouraging the emergence, persistence and dissemination of AMR genes within secondary food processing activities.
14. In the area of animal feed, the group recognised the increasing trend for animal owners to feed their companion animals raw meat based diets (RMBDs) and that RMBDs may be contaminated by enteric pathogens such as *Campylobacter* spp., *E. coli*, *Yersinia* spp. and *Salmonella* spp. all of which are, or potentially are, zoonotic bacteria causing enteritis not only in humans but also in companion animals. The group suggested that it is high priority that further research is carried out on the prevalence of these pathogens in companion animal food and the contribution to human AMR that these pathogens may make.
15. In the area of food-producing animals, it was recommended as high priority that large-scale surveillance studies are carried out at 'macro' level to identify linkages and generate risk-based priorities for more detailed research. Robust insights on linkages between antimicrobial usage in livestock and fish, and prevalence of AMR in food animal bacteria and human consumers of resulting 'products of animal origin' depend on large scale standardised surveillance. Such surveillance should also take account of key contributory factors including human antimicrobial consumption and whether/how the prevalence and diversity of AMR bacteria changes from the food producing animal on the farm or fish farm, during transport and in the abattoir or at processing (including mixing of animals and environmental contamination of transport, lairage and abattoir processing equipment and practice), and beyond.
16. In the area of amendments, it was recommended as high priority that the FSA should consider the risks associated with vegetable crops, especially leaf and root crops and support research to identify high risk crops and quantify those risks.
17. A full list of all high priority recommendations and other recommendations can be found in the report at Annex 1.

Overarching themes

18. During the course of the Task and Finish Group's work, it became apparent that a number of themes were continuously identified across all the sectors being reviewed and the group viewed it as important that these themes are highlighted.
19. Examples of overarching themes identified include the observation that there is a significant lack of antimicrobial and AMR data in relation to UK produced or processed food, or food imported to the UK, both in absolute and comparative terms. Much of the readily available UK AMR data have been obtained indirectly as a consequence of research focussing on themes other than AMR.
20. The need to review consumer education programmes in response to increased risks associated with contact with raw pet foods and consumption of raw drinking milk to limit potential exposure to AMR bacteria was flagged as another theme that crossed several areas.
21. The group identified that there needs to be co-ordinated, regular, targeted surveillance to identify the contribution that food makes to AMR in humans relative to other routes of exposure. It was stressed that this work needs to be joined up across all sectors in an ongoing effort using a "One Health" approach which considers that ultimately, acquisition of AMR in/from food maybe linked to apparently separate activities for example manufacture, waste, disposal etc. Where grey areas are identified in terms of ownership for AMR-related work, there needs to be clarification.

The way forward

22. The Task and Finish report includes a significant number of recommendations. Many of these are cross-cutting in scope reflecting the linkage between different parts of the food chain and with other sources including humans and the environment. This complexity is well illustrated by the systems maps in the Annexes to the report and this highlights the need for the FSA to work with partner organisations including other funders to deliver the science agenda in this area.
23. The need for improved and more joined-up surveillance is a key theme in several of the recommendations. The FSA and other organisations are already undertaking surveillance of AMR bacteria in animals, food and humans but key challenges include improving the robustness and comparability of surveillance data across all sectors and in being able to link these studies together in a way that maximises the opportunity for important cross-cutting questions to be addressed.
24. On AMR bacteria in retail foods, the FSA has prioritised surveillance activities to address key evidence gaps based on the systematic review of the AMR literature (FS102127). We have undertaken well-structured, targeted surveillance of AMR pathogens and commensals in chicken and pork of UK and non-UK origin and in

a way which will enable such studies to be repeated in the future so that trends over time can be examined. However, as evidenced by the systematic review there are other commodities where we have limited data (e.g. fresh produce, dairy, seafood) and a key challenge will be in undertaking repeat studies for certain foods to monitor trends whilst plugging the evidence gaps for others deemed to also be a priority.

25. A further challenge is being able to relate the findings from one part of the food chain (e.g. the retail food studies) to what is happening in supply chains and in food production and the environment. Whilst the FSA is already working with others nationally and internationally there is a need for more co-ordinated partnership working to address the multifaceted nature of the AMR challenge. The FSA will draw this challenge to the attention of other funders (e.g. the MRC funders forum) with a view to developing a framework for how better integrated studies might be conducted and funded as part of a “one health” approach. We will also take the opportunity to draw the report to the attention of the Codex Task Force as it is particularly pertinent to the work on developing guidelines on integrated monitoring and surveillance of foodborne AMR.
26. It is also important to better understand how interventions in the food chain impact on the risk posed by AMR bacteria. Existing farm to fork quantitative risk assessment models developed for foodborne pathogens in specific commodity chains (e.g. *Salmonella* in pork) can be adapted to consider AMR bacteria (pathogens and commensals) particularly for CIAs. This may provide a way to assess the impact of interventions at different points in the food chain notwithstanding the importance of having good quality data to support such models.
27. Work is also needed to improve the evidence base concerning the diverse bacteria (pathogens and commensals) found in the food chain and their relative importance in transmission of AMR compared to other routes, particularly as previous work has tended to focus on human pathogens. In our recent retail survey of chicken and pork we included a range of commensal bacteria (*E.coli*, *Klebsiella* spp., *Enterococcus* spp.) alongside testing for pathogens. In August we published a new research call inviting bids to undertake a study to assess the burden of antimicrobial resistance genes present in bacteria in selected ready-to-eat foods. This work is key to supporting the FSA’s surveillance and risk assessment work on AMR by identifying the nature and extent of such genes so that we can start to quantify their intake through the diet. The work is complimentary to the research we are funding through the fellowship at the Quadram Institute.
28. Several of the recommendations relate to improving our understanding about the role of food processing and there has clearly been a gap in this area with AMR research and surveillance tending to focus on animal production and retail foods. The FSA recently invited proposals to undertake a review of the impact of secondary food processing on the presence and spread of AMR bacteria in meat and meat products.

29. In terms of consumer education, the existing 4Cs (cleaning, cooking, chilling and avoiding cross-contamination) will help in reducing consumer exposure to AMR bacteria through most foods. Government groups have also been discussing safety issues relating to raw meat pet food and ACMSF has suggested including mitigation of risk to humans associated with contact with raw pet foods in the advice/guidance that is published.

Conclusion

30. The Board is asked to:
- **discuss** the report and key recommendations; and, in particular; and
 - **agree** that the report provides an evidence base to inform engagement with other partners including other research funders with whom we will need to work to deliver this agenda.

Annex 1

[Report of the ACMSF Task and Finish Group on AMR](#)

Annex 2

FSA programme of research and surveillance on AMR

This section summarises FSA efforts with respect to AMR research and surveillance, highlighting both completed projects and new and continuing work. Our new and continuing programmes have been influenced by the recommendations of the ACMSF Task and Finnish Group report.

Surveillance completed since December 2017;

- FS102109: Year 2 EU harmonised survey on AMR²
- FS102121: Year 2 Survey of AMR in *Campylobacter jejuni* and *Campylobacter coli* from retail chilled chicken in the UK³
- FS101196: New Retail survey on AMR bacteria in retail chicken and pork mince (<https://www.food.gov.uk/research/foodborne-diseases/surveillance-study-of-antimicrobial-resistance-in-uk-retail-chicken-and-pork#>).

Further survey reports are expected to be published later this year.

Continuing research;

- FS101185: Quadram Institute Fellowship update
 - The FSA is co-funding a five-year Research Fellowship (2017-2022) with the Quadram Institute, Norwich. The FSA contributes via the Strategic Evidence Fund. The Research Fellow, Dr Alison Mather, is investigating food chain transmission of AMR, the relative contribution of imported vs domestic food and the role of non-pathogenic bacteria in food as an AMR reservoir.
 - Work includes a 1-year sampling of retail food in a defined geographical region, comparison with contemporaneous samples from animals and humans in the same region, over the same period (in collaboration with PHE and APHA), and utilisation of sequencing to evaluate the prevalence, diversity, source attribution etc. of pathogens and AMR.
 - The first full year report is due in October, along with a detailed workplan for year two. However, early progress is promising and Dr Mather now has four

² <https://www.food.gov.uk/sites/default/files/media/document/fs102109y2.pdf>

³ <https://www.food.gov.uk/research/research-projects/antimicrobial-resistance-in-campylobacter-jejuni-and-campylobacter-coli-from-retail-chilled-chicken-in-the-uk>

postdoctoral researchers in her team, including a member who is providing insight on comparable retail surveys conducted by the Public Health Agency of Canada. The rapid expansion of her high calibre, international team represents a greater than anticipated return on FSA investment at this early stage.

- Both the CSA and Interim Head of Science attended Quadram Institute's official launch in June, seeking to further develop ties with this centre of excellence. It is anticipated that further projects/partnerships may be developed in the future.

- FS101013: *Campylobacter* Source Attribution & AMR

- Good progress has been made in tackling *Campylobacter* and contamination levels on retail chicken are now lower than several years ago. Contamination levels on retail chicken provide one indicator of progress in tackling this problem but another area the FSA is exploring is through monitoring the proportion of *Campylobacter* clinical isolates which can be attributed to chicken. This is being explored through an FSA project being undertaken by the University of Oxford in collaboration with Public Health England. The project has established sentinel surveillance for human *Campylobacter* infections in rural and urban populations in the Oxford and Tyneside areas and is comparing clinical isolates from these areas to a reference dataset of isolates for key food and animal sources using whole genome sequencing (WGS) and multi-locus sequence typing (MLST).
- This approach is enabling attribution of human cases to food animals and other sources, thereby mapping the contribution to human infection and changes over time. Historical data from Oxfordshire, and by extension ongoing Oxfordshire and Tyneside surveillance, has been shown to be informative on national patterns of human *Campylobacter* infection.
- The FSA has expanded the scope of the existing project to analyse the existing *Campylobacter* sequences (2009-2015) for the presence of antimicrobial resistance genes. This includes fluoroquinolones, macrolides, tetracyclines, aminoglycosides and evidence of multi-resistance (resistance in 3 or more classes of antimicrobials). Sequencing of older human *Campylobacter* isolates (2003-2009) will provide information on trends in antimicrobial resistance over time and this data-rich resource supports models to track the sources and reservoirs of AMR in *Campylobacter* which will help define key risk factors.

New research

- In June 2018 we published a new research call inviting bids to undertake a critical review of the impact of food processing on AMR bacteria in meat & meat products (FS301059). This work is expected to begin by the end of

2018. Most of the FSA's surveillance activities have focussed on the presence of AMR bacteria in raw meat at retail in the UK. However, as highlighted by the ACMSF 'Task and Finish' Group (Annex 1), there is currently a lack of evidence on the impact of secondary food processing on the presence and spread of AMR bacteria in meat and meat products.

- In August 2018 we published a new research call inviting bids to undertake a study to assess the burden of antimicrobial resistance genes in selected ready-to-eat foods (FS301060). This work is key to supporting the FSA's surveillance and risk assessment work on AMR by identifying the nature and extent of AMR genes found in certain key RTE foods so that we can quantify the intake of these through the diet. It will also contribute towards assessing the link between antimicrobial use in agriculture and AMR in people acquired via food.